Case Report

Psychosis as Harbinger of Phenytoin Toxicity

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ABSTRACT

Psychosis with phenytoin use has earlier been reported only in the context of Vitamin B12 or folic acid deficiency. We report a rare case of phenytoin toxicity manifesting as psychosis in the absence of Vitamin deficiency. The importance of recognition of psychosis as a harbinger of phenytoin toxicity and implications for management are discussed.

Key words: Phenytoin, psychosis, toxicity

INTRODUCTION

Phenytoin is the most widely prescribed anti-epileptic in India because of being cheap and widely available.[1] Adverse effects with phenytoin use manifesting in various psychiatric disorders or behavioral symptoms have been reported earlier.[2,3] Psychosis with phenytoin use has earlier been reported only in the context of Vitamin B12 or folic acid deficiency.[4] We report a rare case of phenytoin toxicity manifesting as psychosis in the absence of Vitamin deficiency.

CASE REPORT

A 25-year-old unmarried male educated up to higher secondary with no premorbid mal-adaptive traits was brought to Psychiatry emergency with a history of unmanageable aggression toward family members. Review of history revealed that he had unreasonable suspiciousness toward his mother that she used to poison his food, and would also report hearing of voices of family members conspiring to kill him, along with disturbed sleep for last 20 days. He had a history of recurrent generalized tonic-clonic seizures for last 15 years. He was taking 200 mg per day of phenytoin sodium orally for long time earlier and the dose was increased to 300 mg per day after last seizure episode around 2 months back (i.e., 40 days before onset of psychosis). There was no seizure in last 2 months before presentation. There was no history of fever, head injury, disturbance in the level of consciousness or any substance use.

His physical examination including detailed central nervous system examination showed mild tremors of outstretched hands and titubation (family members denied having noticed it earlier) without any other abnormality. Mental status examination revealed delusions of persecution and reference along with auditory hallucinations (second person with threatening content), with impaired judgment and absent insight. Investigations including complete blood count, liver function tests, renal function tests, fasting blood sugar, serum electrolytes, serum Vitamin B12 and folic acid, X-ray chest (posterior-anterior view), electroencephalograph, and computed tomography Scan

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head did not reveal any abnormality. Oral lorazepam up to 6 mg in divided doses was given for initial few days in order to control marked aggression and was gradually tapered off after 7–10 days. Oral olanzapine 10 mg was started in view of psychotic features and was gradually increased to 30 mg/day over 21 days, but improvement remained unsatisfactory.

In view of poor improvement in psychotic symptoms and worsening of tremors and titubation (suggesting cerebellar signs of phenytoin toxicity) along with slight decrease in level of consciousness, serum phenytoin levels were obtained and were found to be markedly raised (24.9 mcg/ml against reference range of 10–20 mcg/ml). Phenytoin was stopped, and he was started on a combination of sodium valproate and clobazam as antiepileptic. It was respitefully surprising to note that besides improvement in level of consciousness, tremors and titubation; the delusions and hallucinations and aggression secondary to them, which were not responding to olanzapine 30 mg/day even after 5 weeks, started waning off within 2–3 days of stopping phenytoin. Repeat serum phenytoin levels were obtained after 10 days which came down to 19.3 mcg/ml, and again after 2 weeks when it was 12.4 mcg/ml with complete improvement in his psychotic features. Olanzapine was subsequently tapered off after being given for 5 weeks.

After maintaining well for 2 months, the patient again presented in psychiatry OPD with reemergence of psychotic symptoms and tremors and titubation. On review, it was found that the patient had poor control of seizures after stopping sodium valproate and clobazam due to poor affordability. Subsequently, he had been restarted on phenytoin by a Neurologist. The serum phenytoin level was again very high (29.7 mcg/ml). This time he was managed without antipsychotics by just withholding the phenytoin, and all the symptoms disappeared in 7–10 days. Subsequently, he was again prescribed sodium valproate in consultation with treating Neurologist and logistics of follow-up visits, and free dispensing of medication were worked out. He had been symptom-free for at least 6 months thereafter.

DISCUSSION

The patient had presented to Psychiatry emergency with prominent psychotic symptoms. Diagnosis of inter-ictal or postictal psychosis was ruled out, as the index patient was seizure free for a considerably long period, and there was no temporal correlation of psychopathology with seizure episodes. Initially, a possibility of psychosis because of Vitamin B12 or folic acid deficiency arising with the long-term use of phenytoin was kept. However, the serum levels for both were on the higher side of normal limits. A provisional diagnosis of acute and transient psychotic disorder was made as no known organic basis for psychosis could be found, and he was started on olanzapine and lorazepam. However, phenytoin neurotoxicity was suspected on the basis of non improvement and worsening of tremors and titubation and was confirmed by serum phenytoin levels. Removal of phenytoin and decrements in serum levels coincided with the disappearance of psychotic symptoms leading to strong suspicion of psychosis being the initial presentation of phenytoin toxicity. However, the delayed effect of antipsychotic could not be ruled out completely. However, reemergence of psychosis along with tremors and titubation after reintroduction of phenytoin and remission after restopping made it a definite case for psychotic symptoms being a manifestation of phenytoin neurotoxicity. The Naranjo adverse drug reaction probability scale score of 9 indicates that psychosis can be definitely attributed to phenytoin toxicity.[5]

The implied message is that phenytoin toxicity may also present with psychiatric syndromes in the absence of or without prominent neurological symptoms, especially before the levels go high enough to lead to the emergence of neurological symptoms. The emergence of psychosis in a patient taking phenytoin should lead to detailed evaluation for phenytoin toxicity. Management of psychotic symptoms with antipsychotics is not advised as it has been found to be unsuccessful. However, removal of phenytoin can lead to improvement in few days.

This report should not discourage oneself from prescribing phenytoin in the management of epilepsy particularly in a resource poor country like India. The recurrence of seizures due to nonadherence to alternate anti-epileptic because of cost constraints should be seen as a testimony to this advice.

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Conflicts of interest

There are no conflicts of interest.

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